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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,909	12/06/2001	Jay Keasling	2000-0007	1524
23980	7590	09/09/2004	EXAMINER	
REED & EBERLE LLP 800 MENLO AVENUE, SUITE 210 MENLO PARK, CA 94025			FRONDA, CHRISTIAN L.	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,909	KEASLING ET AL.	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-60 is/are pending in the application.
- 4a) Of the above claim(s) 24-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12/6/2201 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restriction

1. Applicants' election of Group I, claims 1-23, in the reply filed on June 14, 2004, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 24-60 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. The requirement is still deemed proper and is therefore made FINAL.
2. Claims 1-23 are under consideration in this Office Action.
3. The rejection of claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps, has been withdrawn in view of applicants' arguments filed June 14, 2004.
4. The rejection of claims 3 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoshino et al. [EP 0955363] in view of Takagi et al. [Journal of Bacteriology, Aug 2000, p. 4153-4157] has been withdrawn in view of applicants' amendments and arguments filed June 14, 2004.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

5. Claims 1-4, 6-8, 10, and 12-23 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants' arguments filed on June 14, 2004, have been considered but are not persuasive. Applicants' position is that the claims as amended recites details of the mevalonate pathway and the roles of the enzymes which is asserted to meet the written description requirement. The examiner respectfully disagrees for reasons of record as supplemented below.

The claims are genus claims encompassing a genus of methods for preparing any isopentenyl pyrophosphate in any host microorganism using any plurality of heterologous nucleic acids of any nucleotide sequence and structure encoding any enzyme of any amino acid sequence

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and structure that carries out the steps (a) to (f) recited in claim 1.

The scope of the claims are highly variant and includes many heterologous nucleic acids with widely differing structural, chemical, and physical characteristics which encode many heterologous enzymes that have widely differing structural, chemical, and physical characteristics which carries out the steps (a) to (f) recited in claim 1.

The specification describes the production of the carotenoid lycopene using an E. coli strain transformed with the MEVT operon of SEQ ID NO: 8 and the MBI operon of SEQ ID NO: 12 and transformation of an E. coli strain MEVT operon of SEQ ID NO: 8 and MEVB operon of SEQ ID NO: 9, where the MEVT and MEVB operons contain a nucleic acid of SEQ ID NO: 1 which encodes a acetoacetyl-coA thiolase, SEQ ID NO: 2 which encodes a HMG-CoA synthase, SEQ ID NO: 3 which encodes HMG-CoA reductase, SEQ ID NO: 4 which encodes mevalonate kinase, SEQ ID NO: 5 which encode phosphomevalonate kinase, and SEQ ID NO: 6 which encode mevalonate pyrophosphate decarboxylase

The specification does not provide a written description of any other genus members other than SEQ ID NO: 1 which encodes an acetoacetyl-coA thiolase, SEQ ID NO: 2 which encodes a HMG-CoA synthase, SEQ ID NO: 3 which encodes HMG-CoA reductase, SEQ ID NO: 4 which encodes mevalonate kinase, SEQ ID NO: 5 which encodes a phosphomevalonate kinase, SEQ ID NO: 6 which encodes a mevalonate pyrophosphate decarboxylase, and SEQ ID NO: 10 which encodes isopentenyl pyrophosphate isomerase.

The method for making the carotenoid lycopene described in the specification, is only representative of a genus of methods for making isopentenyl pyrophosphate using the following transformed microorganisms: (1) a host microorganism transformed with the single operon of SEQ ID NO: 7; (2) a host microorganism transformed with both the MVET operon of SEQ ID NO: 8 and MEVB operon of SEQ ID NO: 9; (3) or a host microorganism transformed with the polynucleotides of SEQ ID NOS: 1-6, where SEQ ID NO: 1 encodes an acetoacetyl-coA thiolase, SEQ ID NO: 2 encodes a HMG-CoA synthase, SEQ ID NO: 3 encodes HMG-CoA reductase, SEQ ID NO: 4 encodes mevalonate kinase, SEQ ID NO: 5 encodes a phosphomevalonate kinase, SEQ ID NO: 6 encodes a mevalonate pyrophosphate decarboxylase, and SEQ ID NO: 10 which encodes an isopentenyl pyrophosphate isomerase.

Thus, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the genus of claim 1. Claims 2-4, 6-8, 10, and 12-23 which depend from claim 1 are also rejected because they do not correct the defect of claim 1.

Amending the claims to recite a method for making isopentenyl pyrophosphate using the following transformed microorganisms may overcome the rejection: (1) a host microorganism transformed with the single operon of SEQ ID NO: 7; (2) a host microorganism transformed with both the MVET operon of SEQ ID NO: 8 and MEVB operon of SEQ ID NO: 9; (3) or a host microorganism transformed with the polynucleotides of SEQ ID NOS: 1-6, where SEQ ID NO: 1

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encodes an acetoacetyl-coA thiolase, SEQ ID NO: 2 encodes a HMG-CoA synthase, SEQ ID NO: 3 encodes HMG-CoA reductase, SEQ ID NO: 4 encodes mevalonate kinase, SEQ ID NO: 5 encodes a phosphomevalonate kinase, and SEQ ID NO: 6 encodes a mevalonate pyrophosphate decarboxylase. Amending claim 13 to recite the proposed host microorganisms in addition to the specific method steps using specific enzymes to make the isoprenoid may overcome the rejection.

Claim Rejections - 35 U.S.C. § 102

6. Claims 1, 12, 22, and 23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hoshino et al. [EP 0955363].

Applicants' arguments filed on June 14, 2004, have been considered but are not persuasive. Applicants' position is that the Hoshino et al. reference does not teach the amended claims since it is asserted that the specific method steps are not disclosed by the Hoshino et al. reference. The examiner respectfully disagrees for reasons of record as supplemented below.

As stated in the previous Office Action Hoshino et al. teach using transformed host cells for the production of product including isopentenyl pyrophosphate containing vectors or plasmids comprising genes encoding enzymes in the mevalonate pathway, where the enzymes encode by SEQ ID NOS: 1-5 are HMG-CoA synthase, HMG-CoA reductase, mevalonate kinase, mevalonate pyrophosphate decarboxylase, and farnesyl pyrophosphate synthase. Hoshino et al. further teach that these genes may be transformed into a host such as E.coli and P. rhodozyma for the purposes of making the carotenoid astaxanthin.

Part (b) of claim 1 is performed by HMG-CoA synthase, part (c) is performed by HMG-CoA reductase, and part (d) is performed by mevalonate kinase, where each of these enzymes is taught by Hoshino et al. as stated above. Although, parts (a), (e), and (f) are not disclosed by Hoshino et al., the transformed host cells taught by Hoshino et al. inherently have the endogenous acetoacetyl-coA thiolase, phosphomevalonate kinase, mevalonate pyrophosphate decarboxylase, which perform the steps of parts (a), (e), and (f). Since the claims as amended do not exclude the endogenous enzymes of acetoacetyl-coA thiolase, phosphomevalonate kinase, mevalonate pyrophosphate decarboxylase, which perform the steps of parts (a), (e), and (f), the Hoshino et al. reference anticipates the invention of claims 1, 12, 13, 22, and 23.

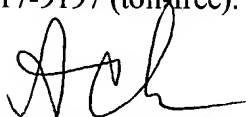
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Conclusion

7. No claim is allowed.
8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.
9. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.
10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF


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